

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

ELSEVIER

Contents lists available at ScienceDirect

## Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres



# Affective psychosis after COVID-19 infection in a previously healthy patient: a case report



Andres F Correa-Palacio\*, Daniel Hernandez-Huerta, Jorge Gómez-Arnau, Carmen Loeck, Irene Caballero

Psychiatry Department, Ramon y Cajal University Hospital, Madrid, Spain

Dear Editor,

At the time this letter is being written, the coronavirus disease 2019 (COVID-19) pandemic has affected more than 3,7 million people around the world. Spain is one of the countries hardest hit by the disease, with more than 250.000 infected and more than 25.000 deaths (Arango, 2020). Since there is no vaccine or specific anti-viral drug to treat COVID-19, several regimens are being empirically administered. It is important to highlight that these treatments used for COVID-19 could induce neuropsychiatric adverse effects.

Neurotropism for the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has also been established. It is clinically more evident when severe respiratory distress is present and manifests with dizziness, headache, ataxia, delirium, agitation, corticospinal tract signs, dysexecutive syndrome, encephalitis and acute cerebrovascular disease (Mao et al., 2020). Although reactive psychoses in this context have also been described (Valdés-Florido et al., 2020), no primary psychiatric disorder with a clear causal relation with COVID-19 has been informed.

Here we report the case of a patient recovering from COVID-19 and with no history of mental illness, who presented a manic episode with psychotic features.

A 43-year-old male patient was brought by the police to our emergency department during COVID-19 outbreak in Spain. No history of allergies and no previous medical conditions were recorded. Regarding substances abuse, he recognized ocassional cocaine use but claimed about being abstinent for the last two weeks before hospitalization. No other personal or family history of mental disorders was reported. Police was called by patient's wife because he was more irritable and restless after being hospitalized for COVID-19. The patient was verbally and physically aggressive and used two swords he had in his house to fend himself off from being arrested.

Prior to this episode, the patient had been treated in the internal medicine department for 8 days as he had presented a bilateral pneumonia with mild respiratory insufficiency related to SARS-CoV-2 infection. He received treatment with oral lopinavir-ritonavir and hydroxychloroquine during these 8 days. The clinical response was good

after the introduction of methylprednisolone at high doses. He did not need supplementary oxygen. The only remarkable finding in blood analysis was hyperglycemia, which was related to corticosteroid treatment. At discharge, 32 mg/day of methylprednisolone were prescribed during 4 more days. At the time the patient came to the emergency department, he was not taking corticoids any longer.

Physical examination at the emergency department revealed no pathological findings. He had neither fever nor dyspnea. A brain CT was reported not observing intracranial acute pathology. Urine toxic screening was negative for cocaine, cannabis, opioids and benzodiazepines. A blood analysis showed a mild renal failure that improved with intravenous hydration and mild leukocytosis that was presumed to be in relation to agitation, since the following day it decreased to normal values. No other acute-phase reactants were altered.

Admission to our psychiatric inpatient unit was required for behavior management. An initial psychiatric evaluation was made, observing a hyperalert oriented patient, who was collaborative but with a moderate level of psychomotor restlessness. His speech was loud, reiterative and logorrheic, with megalomaniac beliefs of "communicating directly with God", and persecutory delusions with medical and police staff. He was expansive and anxious with a high level of self-perceived energy. Visual and auditory hallucinations were recognized by the patient as well as eight-day global insomnia.

During hospitalization, a brain MRI was performed, showing no pathological results. Neurologic exam was normal. A new SARS-CoV-2 PCR test was negative. The probability of encephalopathy of any type was therefore considered low.

He had a full-recovery after 1 month hospitalized. At discharge, he was taking valproic acid 500 mg/8h, paliperidone 15 mg/day, olanzapine 5 mg/day and lorazepam 1 mg PRN. A diagnosis of substance/medication-induced manic episode with psychotic features was issued.

This case report illustrates the potential of COVID-19 and its specific treatments to cause severe psychopathology in a complex way. The first etiological hypothesis was a corticosteroid-induced affective psychosis, since these effects are well reviewed in medical literature (Dubovsky et al., 2012). However, neuropsychiatric side-effects of hydroxychloroquine and antivirals cannot be ruled out. Indeed,

<sup>\*</sup> Corresponding author at: Psychiatry Department. Carretera Colmenar Viejo, Km 9,100. 28024 Madrid, Spain. E-mail address: andresfelipe.correa@salud.madrid.org (A.F. Correa-Palacio).

hydroxychloroquine use has been related to agitation, emotional lability and irritability (Mascolo et al., 2018). Besides, his occasional cocaine use may have influenced the affective psychotic episode, despite of a negative result in urine drug test.

It is also unknown if neuroinflammation or direct virus neurotropism, with subsequent neuronal injury, could have also mediated the neuropsychiatric symptoms, even in the absence of identifiable structural damage on neuroimaging.

All these variables pose a major challenge and difficult the diagnostic process in COVID-19 patients with psychiatric symptoms. That is why as the pandemic goes on, clinicians should make an exhaustive appraisal in order to discard that these symptoms are not secondary to medications. The hypothesis that SARS-CoV-2 infection may directly cause behavioral manifestations is one of the most challenging subjects of study in this field.

### **Funding**

No funding was received for this work.

### CRediT authorship contribution statement

Andres F Correa-Palacio: Writing - original draft, Writing - original draft. Daniel Hernandez-Huerta: Writing - original draft. Jorge

**Gómez-Arnau:** Writing - original draft. **Carmen Loeck:** Writing - original draft. **Irene Caballero:** Writing - original draft.

### **Declaration of Competing Interest**

None.

#### References

- Arango, C., 2020. Lessons learned from the coronavirus health crisis in Madrid, Spain: How COVID-19 has changed our lives in the last two weeks. Biol. Psychiatry. https://doi.org/10.1016/j.biopsych.2020.04.003.
- Dubovsky, A.N., Arvikar, S., Stern, T.A., Axelrod, L., 2012. The neuropsychiatric complications of glucocorticoid use: steroid psychosis revisited. Psychosomatics 53, 103–115. https://doi.org/10.1016/j.psym.2011.12.007.
- Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Miao, X., Li, Y., Hu, B., 2020. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol. https://doi.org/10.1001/jamaneurol.2020.1127.
- Mascolo, A., Berrino, P.M., Gareri, P., Castagna, A., Capuano, A., Manzo, C., Berrino, L., 2018. Neuropsychiatric clinical manifestations in elderly patients treated with hydroxychloroquine: a review article. Inflammopharmacology 26, 1141–1149. https:// doi.org/10.1007/s10787-018-0498-5.
- Valdés-Florido, M.J., López-Díaz, Á., Palermo-Zeballos, F.J., Martínez-Molina, I., Martín-Gil, V.E., Crespo-Facorro, B., Ruiz-Veguilla, M., 2020. Reactive psychoses in the context of the COVID-19 pandemic: Clinical perspectives from a case series. Rev. Psiquiatr. Salud Ment. https://doi.org/10.1016/j.rpsm.2020.04.009.